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ACCURATUM: improved calcium volume scoring using a mesh-based algorithm-a phantom study

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Abstract To overcome the limitations of the classical volume scoring method for quantifying coronary calcifications, including accuracy, variability between examinations, and dependency on plaque density and acquisition parameters, a mesh-based volume measurement method has been developed. It was evaluated and compared with the classical volume scoring method for accuracy, i.e., the normalized volume (measured volume/ground-truthed volume), and for variability between examinations (standard deviation of accuracy). A cardiac computed-tomography (CT) phantom containing various cylindrical calcifications was scanned using different tube voltages and reconstruction kernels, at various positions and orientations on the CT table and using different slice thicknesses. Mean accuracy for all plaques was significantly higher ($p < 0.0001$) for the proposed method (1.220 ± 0.507) than for the classical volume score (1.896 ± 1.095). In contrast to the classical volume score, plaque density

($p = 0.84$), reconstruction kernel ($p = 0.19$), and tube voltage ($p = 0.27$) had no impact on the accuracy of the developed method. In conclusion, the method presented herein is more accurate than classical calcium scoring and is less dependent on tube voltage, reconstruction kernel, and plaque density.

Keywords Coronary calcium · Volume · Computed tomography

Introduction

The determination of coronary atherosclerotic plaque morphology and plaque burden is important for optimized risk stratification and for monitoring coronary disease [1]. In particular coronary calcium, being intimately associated with vascular injury and atherosclerotic plaque formation, represents a strong indicator for coronary atherosclerosis

[2]. Moreover, the quantity of calcification is a strong predictor for the prognosis of the patient with regard to the development of non-fatal and fatal cardiovascular events [3, 4].

Assessment of coronary calcification is performed with computed tomography (CT), where calcium strongly attenuates X-rays because of its high atomic number and thus appears bright on the CT image. Traditionally the

method described by Agatston and coworkers [5] that selects the maximum calcium density within an area of at least three adjacent voxels with a density larger than 130 Hounsfield units (HU) is used for quantification. It accumulates slice-wise the product of plaque area and a factor f that depends on the peak-intensity value within the plaque area. Although most existing patient data are based on Agatston scoring, this method has limitations, particularly regarding the considerable variability between examinations of up to 43% [6–11].

Another method for quantifying coronary calcium is based on the absolute mass [12–14]. To obtain absolute values for calcium mass, a calibration measurement of a calcification with known hydroxyapatite density has to be performed and a calibration factor needs to be determined. Recently, the volume score method was introduced [15], which is based on the product of the number of voxels containing calcium and the volume of one voxel. As compared to the Agatston method, the volume score has reduced the variability between examinations to some degree [6–8, 10], however, it also has limitations. The volume score is vulnerable to overestimation of lesion size owing to partial volume effects. Objects smaller than one voxel contribute to the score with the entire voxel volume, and the volume score, which depends on the applied threshold, does not necessarily represent the true volume of calcium [6, 11, 16–18].

The purpose of our study was to introduce and to evaluate a mesh-based algorithm providing a better calcium volume measure with regard to accuracy, variability between examinations, dependency on plaque density, and acquisition parameters in comparison with the classical volume score.

Material and methods

The proposed method was developed and evaluated on a cardiac CT phantom (QRM, Moehrendorf, Germany, www.qrm.de), previously described in detail [6, 12, 14, 19, 20]. The phantom consisted of an anthropomorphic body and a calibration insert containing three sets of calcified cylinders. The longitudinal axis of each cylinder was parallel to the phantom's longitudinal axis. The plaque equivalents were made of hydroxyapatite (HA) with the characteristics shown in Table 1. Unless otherwise stated, the phantom was aligned on the scanner table with its longitudinal axis parallel to the scanner's z-axis.

All CT examinations were performed on a dual-source CT system (Somatom Definition, Siemens Medical Solutions, Forchheim, Germany) with a detector collimation of $2 \times 32 \times 0.6$ mm and a slice acquisition of $2 \times 64 \times 0.6$ mm by means of a z-flying focal spot [21]. A slice spacing equal to the slice thickness was chosen for all CT data acquisitions. Following a standard calcium scoring protocol, a pitch of 0.2 and a tube current-time product of 80 mAs were

Table 1 Density, length, diameter, volume, and mass for each of the nine plaque equivalents that are inside the cardiac CT phantom

| Label for this study | Density (mg/cm ³) | Length/diameter (mm) | Volume (mm ³) | Mass (mg) |
|----------------------|-------------------------------|----------------------|---------------------------|-----------|
| 1 | 200 | 5.0 | 98.2 | 19.6 |
| 2 | 200 | 3.0 | 21.2 | 4.2 |
| – | 200 | 1.0 | 0.8 | 0.2 |
| 3 | 400 | 5.0 | 98.2 | 39.3 |
| 4 | 400 | 3.0 | 21.2 | 8.5 |
| – | 400 | 1.0 | 0.8 | 0.3 |
| 5 | 800 | 5.0 | 98.2 | 78.5 |
| 6 | 800 | 3.0 | 21.2 | 17.0 |
| – | 800 | 1.0 | 0.8 | 0.6 |

Only plaque equivalents used for this study were assigned a numerical label for referencing purposes

selected. A field of view of 170 mm led to an in-plane pixel size of 0.332 mm. The CT system was calibrated with room-temperature air immediately before the phantom measurements.

Training data sets

A first series of data sets (in the following referred to as set A_i) was acquired by scanning the phantom with four different tube voltages (i.e., 80, 100, 120, and 140 kV) without changing its position on the CT table between the examinations. Each acquisition was reconstructed with an effective slice thickness of 3 mm using four different reconstruction kernels (B30f, B35f, B46f, B50f), resulting in a total of 16 data sets. This series was used to assess the accuracy of the volume measurement and its dependency on scanning parameters.

A second series of data sets was acquired to assess the variability of the measurements between examinations. The phantom was examined 10 times with constant parameters (i.e., 120 kV, B35f) at arbitrarily chosen positions along the z-axis of the CT table. The images were reconstructed with an effective slice thickness of 3 mm (denoted as set B_i) and 1 mm (denoted as set C_i).

These three sets (A_i , B_i , C_i) were used for the development and parameter optimization of the proposed algorithm and are subsequently called *training* data sets.

Evaluation data sets

All CT examinations as described before were repeated on the same day. These resulting *evaluation* data sets (A_e , B_e , C_e) were used for the evaluation of the proposed algorithm. Additional evaluation data sets were acquired by varying the orientation of the phantom on the CT table with constant CT parameters (i.e., 120 kV, B35f). For one fixed

position, the phantom was rotated around the y -axis of the CT system in 10° steps starting from 0° (i.e., the phantom's longitudinal axis was parallel to the CT table's z -axis) to 90° . The resulting 10 examinations were reconstructed with an effective slice thickness of 3 mm (denoted as set D_e) and 1 mm (denoted as set E_e).

Calcium scoring

The Agatston score, the mass score, and the volume score were calculated as aforementioned from all data sets on an external workstation (Multimodality Workplace, Siemens) equipped with cardiac post-processing software (Calcium Scoring, Siemens) for calcium scoring.

ACCURATUM

The developed algorithm (Fig. 1, steps 1–5) presented herein is subsequently referred to as ACCURATUM (A Calcium sCoring volUme measuRe - Accurate Through Using Meshes). To overcome the voxel as a discrete unit for volume measurements, each plaque is converted into a mesh (Fig. 1, step 1) such that its nodes n_i , representing the boundary between plaque and surrounding tissue, could be arbitrarily positioned in space, independently from the underlying voxels. As the position of this boundary is affected by the scanning characteristics of a CT system, the intensity profile along the surface normal of each node n_i (Fig. 2) was evaluated to determine the real position of the boundary.

In a first approximation, a CT system can be described as a linear shift invariant system such that its degenerative effect (such as the blurring of edges) can be described by a

convolution of the input image with a system-specific transfer function $t(x,y,z)$:

$disturbed(x, y, z)$

$$= \int \int \int input(x, y, z) t(x - u, y - v, z - w) du dv dw$$

Hence, it would be desirable to reverse this process by applying the inverse transfer function on the CT image (deconvolution). However, this deconvolution is mathematically unstable. So instead of deconvolving, ACCURATUM convolved ideal boundaries between two materials A and B with the transfer function (step 3) and compared them with the extracted intensity profile (step 4). The ideal boundary with the minimum squared error to the intensity profile was taken, and the corresponding node n_i was repositioned to the location of the ideal boundary (step 5). In more detail, the five steps of ACCURATUM are as follows (see Fig. 1):

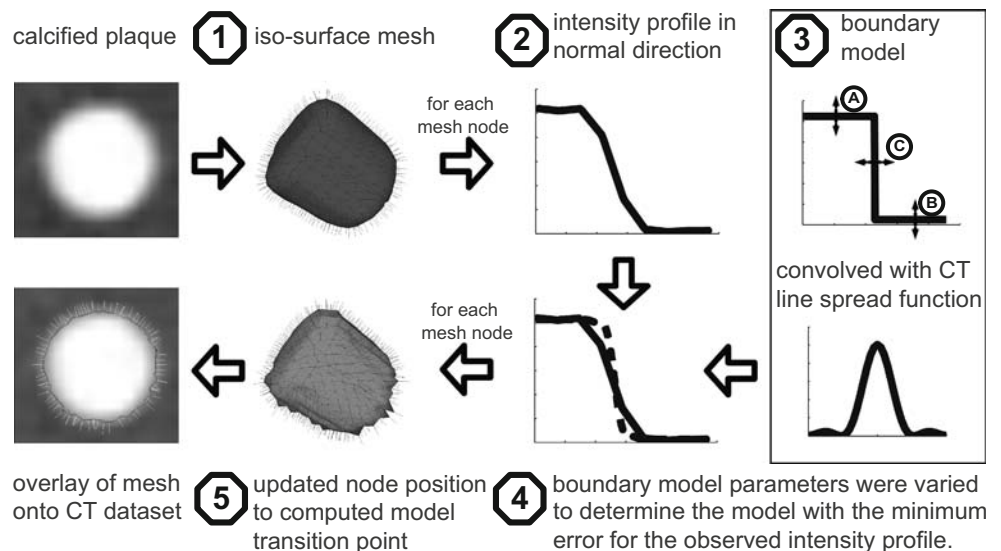
Step 1

An iso-mesh representation of the calcified plaque using a marching cube algorithm was computed. The mesh was initialized with an iso-value defined by the mean intensity of the plaque according to the 130 HU threshold criterion of the Agatston score. If the mean intensity was below a threshold t_m and the 75%-quantile intensity was below a threshold t_q , ACCURATUM was not applied and the calcium scoring volume was taken.

Step 2

The intensity profile of each node n_i along its surface normal direction in the xyz -coordinate system was extracted.

Fig. 1 ACCURATUM uses a mesh-based representation for the calcified plaque to determine the position for each mesh node that most likely represents the boundary between the plaque and the surrounding tissue



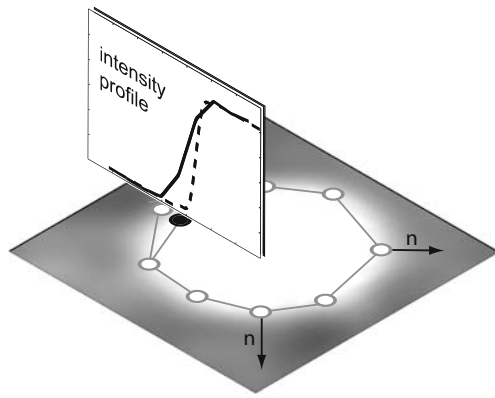


Fig. 2 The intensity profile is computed for each node along its normal direction n . The position of the node is updated to the boundary point (filled circle) obtained by fitting a boundary model (dotted line) to the measured intensity values (solid line) in the intensity profile

Step 3

A set of ideal boundaries was convolved with the transfer function described by an isotropic (independent from the direction) line-spread function (LSF). The ideal boundaries were varied in the intensities for both materials A and B as well as in the position C of the boundary. Based on previous research results [22], a $[\sin(x)/x]^2$ function was chosen for the LSF.

Step 4

The sum of absolute differences (SAD) was calculated between each node's intensity profile and the set of convolved ideal boundaries. The ideal boundary with the minimum SAD was chosen.

Step 5

Each node n_i was repositioned to the location of its ideal boundary. After processing all nodes n , the volume of the final mesh was computed.

The parameters of ACCURATUM, i.e., thresholds t_m and t_q , were manually selected using the training data sets to optimize the accuracy and variability between examinations. ACCURATUM was developed and evaluated using the Windows operating system on a Pentium 4 with 3 GHz and 2 GB RAM as a module for MeVisLab (version 1.5, Software for Medical Image Processing and Visualization, www.mevislab.de). The code was written in C++ for Visual Studio.

Statistical analysis

All statistical analysis was performed using the freely available statistical software package R (Version 2.2.0 for Windows). Quantitative variables were expressed as mean (\pm standard deviation) and categorical variables as percentages.

The calcium scoring volume and ACCURATUM were compared regarding the accuracy of the measurements.

Accuracy was defined as the ratio between measured volume and the ground-truthed volume. An accuracy >1 represented an overestimation, whereas an accuracy <1 represented an underestimation of the plaque volume. Variability was defined as the standard deviation of a measurement. Variability in scores for a single plaque between examinations was defined as the standard deviation of its accuracy. The variability in scores of a group of plaques was defined as the mean of the variabilities from the individual plaques. Set A_e was taken to evaluate the dependency of both volume measures on the tube voltage and the reconstruction kernel. The variability of both volume measures was determined using data set $B_e - E_e$. Analysis of variance (ANOVA) was used on set $A_e - E_e$ to statistically compare the accuracy of ACCURATUM with the calcium scoring volume method. A multivariate analysis of variance (MANOVA) was used on set A_e to evaluate the dependency of both volume measures on the plaque density, reconstruction kernel, and tube voltage. On set $B_e - E_e$, a paired Student's t -test was used to compare the mean accuracy and the variabilities of the different plaques between examinations.

Results

Similar to previous studies [6, 12, 20], the plaque equivalent cylinders with a diameter of 1 mm were not clearly discernible in most of the data sets. Only the most calcified plaques in the 1-mm reconstruction could be consistently analyzed. The Agatston score and mass were computed for completeness (Supplementary Table 1) but were not further analyzed.

Training data sets

For all 3-mm training data sets (sets A_t and B_t), the parameters for ACCURATUM were set to $t_m=200$ HU and $t_q=300$ HU, whereas for all 1-mm data sets (set C_t), the parameters were selected as $t_m=220$ HU and $t_q=300$ HU. These values were then used for the measurements in the evaluation data sets. It has been observed that an individual parameter set for each slice thickness allows a more precise optimization, although one set of global parameters would be desirable. This step was justified because, in general, only a small number of possible slice thicknesses occur for which ACCURATUM would have to be calibrated.

Evaluation data sets

In the following, both volume measures were evaluated with regard to their dependency on the CT parameters,

namely tube voltage and reconstruction kernel, and for their variability between examinations.

Scan parameters

Set A_e was used to investigate the dependency of the volume measures on the CT parameters. Averaging over all plaques of this set showed a significant decrease ($p=0.001$) in the accuracy for the volume score with decreasing tube voltages (80 kV: 3.060 ± 2.674 , 140 kV: 1.839 ± 0.888). The tube voltage, however, had no impact ($p=0.27$) on the accuracy of ACCURATUM (80 kV: 1.407 ± 1.223 , 140 kV: 1.168 ± 0.315). A significant decrease ($p<0.001$) in the accuracy could be observed for the volume score when changing from a soft (B30f) to a sharp (B50f) reconstruction kernel. ACCURATUM proved to be more robust ($p=0.19$) against the different reconstruction kernels. The volume score significantly depended on the plaque density ($p<0.0001$), whereas ACCURATUM showed no significant dependency on plaque density ($p=0.84$).

Variability between examinations

The variability was evaluated with constant scan parameters by translating the phantom along the z-axis of the CT system (set B_e and C_e) and by rotating it around the y-axis of the CT table (set D_e and E_e) for a fixed position.

Variability between examinations - translation

For the 3-mm data sets (set B_e), ACCURATUM (1.330 ± 0.544) was significantly ($p<0.0001$) more accurate than the calcium volume method (1.862 ± 0.925) in terms of the mean accuracy over all plaques. Over the 10 scans for the plaques in set B_e, ACCURATUM had a variability of ± 0.261 , whereas the volume score had a variability of ± 0.121 , with significant differences between the methods ($p=0.036$).

For the 1-mm data sets (set C_e), ACCURATUM (1.082 ± 0.121) was also significantly ($p<0.0001$) more accurate than the volume score (1.651 ± 0.558) for the mean accuracy over all plaques. ACCURATUM (± 0.051) had a variability similar ($p=0.192$) to the volume score method (± 0.081).

Variability between examinations - rotation

Similar results were obtained while rotating the phantom. For the 3-mm data sets (set D_e), the proposed method (1.361 ± 0.571) was significantly ($p<0.0001$) more accurate than the calcium volume method (1.847 ± 0.973) over all plaques. Over the 10 scans for the plaques in set D_e,

ACCURATUM had a variability of ± 0.179 , whereas the volume score had a variability of ± 0.080 , with non-significant differences between the methods ($p=0.143$).

For the 1-mm data sets (set E_e), ACCURATUM (1.095 ± 0.138) was also significantly ($p<0.0001$) more accurate than the volume score (1.651 ± 0.557) for the mean accuracy over all plaques. ACCURATUM (± 0.051) had a variability similar ($p=0.157$) to the volume score method (± 0.061).

Slice thickness

A reduction in the effective slice thickness from 3 mm (set B_e, D_e) to 1 mm (set C_e, E_e) led to a significant improvement in the accuracy ($p<0.0001$) and variability ($p<0.0001$) for both volume scores.

The dependency of both measures on the plaque density (set B_e - set E_e) is shown in Fig. 3. For the 3-mm data sets, medium and highly calcified plaques (plaques 3–6) were heavily overestimated by the volume score method whereas ACCURATUM was less dependent on the plaque density. For an effective slice thickness of 1 mm, the proposed method was even more robust ($p=0.32$) towards differing plaque densities.

A detailed overview of all volume measures can be found in Table 2 where ACCURATUM and the volume score were compared separately for the five data sets and the six plaques.

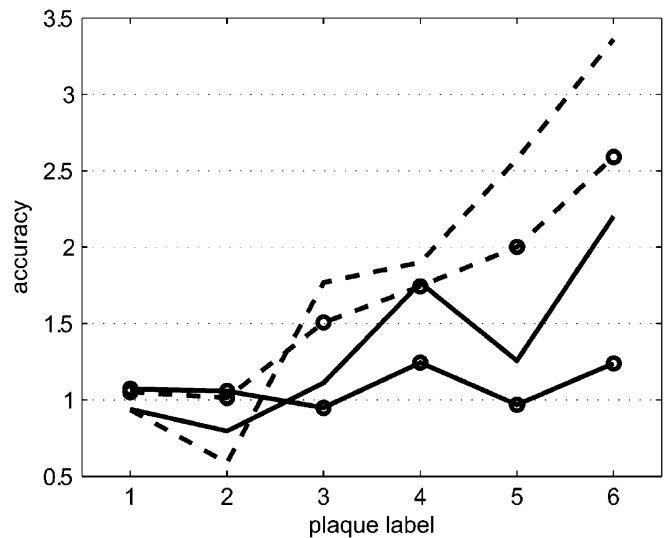


Fig. 3 For each plaque, the mean accuracy was computed. ACCURATUM (solid line) was less dependent on the plaque density for 3-mm slices than the volume score (dashed line). Better results for both methods could be achieved by using a slice thickness of 1 mm (lines marked with circles) instead of a slice thickness of 3 mm

Table 2 The mean accuracy (\pm standard deviation) of the conventional volume score (CVS) and ACCURATUM (ACC) was evaluated for each considered plaque within the phantom for the evaluation data sets (sets A_e, B_e, C_e, D_e, and E_e)

| Label | Set A _e | | Set B _e | | Set C _e | | Set D _e | | Set E _e | |
|-------|--------------------|-------------|--------------------|-------------|--------------------|-------------|--------------------|-------------|--------------------|-------------|
| | CVS | ACC | CVS | ACC | CVS | ACC | CVS | ACC | CVS | ACC |
| 1 | 1.167 \pm | 0.793 \pm | 0.954 \pm | 0.897 \pm | 1.048 \pm | 1.066 \pm | 0.916 \pm | 0.984 \pm | 1.055 \pm | 1.077 \pm |
| | 0.310 | 0.184 | 0.091 | 0.292 | 0.050 | 0.054 | 0.047 | 0.070 | 0.036 | 0.042 |
| 2 | 1.383 \pm | 1.418 \pm | 0.643 \pm | 0.836 \pm | 1.026 \pm | 1.077 \pm | 0.535 \pm | 0.756 \pm | 1.003 \pm | 1.039 \pm |
| | 1.394 | 1.492 | 0.123 | 0.168 | 0.045 | 0.063 | 0.117 | 0.135 | 0.086 | 0.091 |
| 3 | 1.927 \pm | 1.032 \pm | 1.773 \pm | 1.116 \pm | 1.504 \pm | 0.950 \pm | 1.765 \pm | 1.106 \pm | 1.508 \pm | 0.948 \pm |
| | 0.274 | 0.080 | 0.079 | 0.175 | 0.068 | 0.066 | 0.047 | 0.137 | 0.048 | 0.038 |
| 4 | 2.546 \pm | 1.415 \pm | 1.931 \pm | 1.800 \pm | 1.744 \pm | 1.220 \pm | 1.869 \pm | 1.734 \pm | 1.745 \pm | 1.269 \pm |
| | 2.190 | 0.191 | 0.122 | 0.303 | 0.089 | 0.046 | 0.067 | 0.183 | 0.061 | 0.053 |
| 5 | 2.730 \pm | 1.035 \pm | 2.534 \pm | 1.245 \pm | 1.989 \pm | 0.959 \pm | 2.619 \pm | 1.269 \pm | 2.013 \pm | 0.977 \pm |
| | 0.475 | 0.107 | 0.116 | 0.108 | 0.071 | 0.030 | 0.072 | 0.053 | 0.041 | 0.019 |
| 6 | 3.765 \pm | 1.655 \pm | 3.339 \pm | 2.089 \pm | 2.598 \pm | 1.221 \pm | 3.380 \pm | 2.316 \pm | 2.584 \pm | 1.257 \pm |
| | 1.964 | 0.147 | 0.193 | 0.519 | 0.161 | 0.046 | 0.134 | 0.497 | 0.094 | 0.061 |

Discussion

This paper introduces ACCURATUM, a method for measuring calcified plaque volume that outperformed the classical volume scoring method in a phantom study. The algorithm proposed here achieved an improved accuracy as compared to the classical volume score. In addition, ACCURATUM was more robust against changes in the plaque density, the reconstruction kernel, and the tube voltage settings.

We concentrated in this study on the improvement of the classical volume score as it can also be used to extract shape information from a plaque. Known limitations of the classical volume measure are its dependency on the plaque density [6], the reconstruction kernel [23, 24], and the tube voltage [25], and its high variability [8, 17]. Lower tube voltages result in higher attenuation coefficients for hydroxyapatite [26] and therefore increase the blurring by the line-spread function, which in turn causes an overestimation of the plaque volume. Thomas et al. [25] showed the impact of two different tube voltages on the intensity values of a calcium insert. As the volume score is defined through a fixed 130 HU threshold, different HU values have a direct influence on its outcome. The dependency of the classical volume measure on the choice of the reconstruction kernel could be also shown in this study, in that additional noise through the usage of sharper reconstruction kernels led to a decrease in the accuracy for the calcium scoring volume measure.

ACCURATUM overcame the limitations of the classical volume score by being more accurate and less dependent on the scanner parameterization measures, such as the tube voltage. Therefore, ACCURATUM is theoretically suitable for the low-dose 80 kV protocol recently proposed by Thomas and coworkers [25]. In contrast to the classical calcium scoring algorithm by these authors, which required adaptation of the threshold, ACCURATUM can be

applied without any algorithm and parameter changes. ACCURATUM was also robust against variations in the reconstruction kernel and did not show the typical decrease in the accuracy with the use of sharper reconstruction kernels as recently observed by Cademartiri et al. [24]. The evaluation using the standard scanning protocol showed an enormous overestimation for the volumes of highly calcified plaques with the classical volume score, whereas ACCURATUM was less dependent on the plaque density. The use of an effective slice thickness of 1 mm led to a significant improvement in accuracy and variability for both ACCURATUM and for the volume score. This effect has already been reported for the volume score [27]. Thus, the use of 1-mm slices for measurements of plaque volumes can be recommended.

Dehmeshki et al. [28] proposed another approach for the volume measurement of calcified plaques. Their algorithm used a modified expectation maximization of a statistical model for the plaque volume measurement. An average error of 9.5% with a standard deviation of 5–20% was achieved on a cardiac phantom. However, as Dehmeshki et al. [28] used a 16-slice CT system and some CT protocols that were not completely defined, a direct comparison with our results was not feasible.

Rollano-Hijarrubia et al. [29, 30] evaluated methods for the quantification of plaques on phantoms such as the 50% relative threshold of the object maximum attenuation value. They could show a reduced measurement variability between examinations and protocols and an increased measurement accuracy with respect to the standard quantification methods. A direct benchmark comparison of all available methods for the quantification of calcified volumes on the same data sets would therefore be desirable but beyond the scope of this paper.

ACCURATUM has two parameters. For their determination, a common approach from the machine learning community has been used: only plaques from the training

sets were considered to calibrate these parameters, whereas the evaluation itself was done exclusively on the evaluation sets. As only phantom scans from a single CT system were available, no conclusion can be drawn as to whether the obtained parameters are directly transferable to other CT systems or if the proposed algorithm has to be calibrated once on each CT system.

The proposed method is initialized by a single click into a calcified plaque. Its volume is then automatically computed within an average time of 1–2 s. A plaque may be surrounded by different tissues as the optimal boundary transition between the plaque and its surroundings is computed for each mesh node separately. We also applied the proposed method to a highly calcified 1-mm plaque that was only visible in the 1-mm reconstructions. ACCURATUM, however, performed (4.530 ± 1.557) no better than the classical volume score (4.003 ± 1.155) as the convolution approach requires a minimum object size such that opposite boundaries do not influence each other. Extracting only the mesh (step 1 of ACCURATUM) and taking the resulting volume led to an accuracy of 1.501 ± 0.373 . So future work will concentrate on defining criteria to

automatically determine when the convolution approach is likely to fail and therefore only the mesh extraction should be applied.

Our study had limitations. First, no moving coronary plaque phantom [31] was used, so potential motion artifacts could not be considered in our study. Second, only cylindrical shapes were evaluated, which most likely do not represent the realistic configuration of coronary plaques in patients. Finally, the presented algorithm could not be verified in an in-vivo setting as appropriate ground-truthed volume data for the calcified plaques were not available.

In conclusion, this phantom study introduces a mesh-based algorithm that is more accurate and in particular more robust than the classical volume scoring method. Further studies should aim at a verification of the herein proposed method both ex vivo and in vivo.

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